IVACG STATEMENT

Status of the Studies on Vitamin A and Human Immunodeficiency Virus Infection

Despite the lack of evidence that vitamin A supplementation can reduce vertical transmission of HIV, there is still an enormous burden of morbidity and mortality related to vitamin A deficiency in sub-Saharan Africa and other areas of the developing world. Control of vitamin A deficiency remains an important health intervention.

International Vitamin A Consultative Group

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At the present time there is not conclusive evidence to recommend the use of vitamin A supplementation as disease-targeted therapy for HIV infection.

Although epidemiological studies suggest that there is an association between vitamin A status and mother-to-child transmission of human immunodeficiency virus (HIV) infection, recent clinical trials have not shown a significant impact of vitamin A supplementation on mother-to-child transmission of HIV. Other epidemiological studies have suggested an association between vitamin A status and morbidity and mortality of HIV infection. At the present time there is not conclusive evidence to recommend the use of vitamin A supplementation as disease-targeted therapy for HIV infection. Studies are currently in progress to determine whether vitamin A supplementation can postpone infant and young child mortality during HIV infection.

Several studies in adults suggest that vitamin A deficiency may be associated with increased clinical progression of HIV infection (1,2) and increased mortality (3). Low plasma vitamin A concentrations during pregnancy have been associated with increased mother-to-child transmission of HIV (4,5), but this association has not been consistently observed across studies (6,7). Among HIV-infected pregnant women, low plasma vitamin A concentrations have also been associated with low birth weight (7,8) and increased infant mortality (8). Studies in Kenya show that low plasma vitamin A concentrations in HIV-infected women are associated with higher HIV load in the vagina (9, 10) and higher detectable HIV in breast milk (11).

Clinical trials were conducted in Tanzania, Malawi, and South Africa to determine whether vitamin A or micronutrient supplementation during pregnancy could reduce mother-to-child transmission of HIV. Antenatal vitamin A and beta-carotene supplementation had no apparent impact upon mother-to-child transmission of HIV in Durban, South Africa (12). Vitamin A supplementation and/or multiple micronutrient supplementation had no impact on mother-to-child transmission of HIV in Tanzania (W. Fawzi, personal communication). In Tanzania, supplementation with multiple micronutrients—but not vitamin A alone—was found to reduce fetal deaths and prematurity (13). In Malawi, vitamin A supplementation to HIV-infected pregnant women reduced the incidence of low birth weight by about one-third but had no significant impact on mother-to-child transmission of HIV (N. Kumwenda, personal communication). These studies suggest that vitamin A supplementation has no effect upon mother-to-child transmission of HIV. In Zimbabwe a clinical trial is currently in progress with both HIV positive and HIV negative mothers and their infants to determine whether vitamin A supplementation soon after delivery will (1) reduce HIV transmission during breast feeding, (2) reduce sexually acquired HIV infection among post partum women, and (3) reduce morbidity and/or mortality among all women and infants.

The role of vitamin A supplementation for HIV-infected children has been explored in studies in South Africa and

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Tanzania. In a trial in South Africa, a stratified analysis involving a subsample of 28 HIV-infected infants suggested that periodic, high dose vitamin A supplementation reduced diarrheal morbidity (14). In Tanzania, a clinical trial was designed to determine whether vitamin A supplementation could reduce morbidity and mortality of acute lower respiratory infections (ALRI) in children. This study showed no overall impact of vitamin A supplementation upon ALRI morbidity and mortality. A stratified analysis among a subsample of 58 HIV seropositive children showed that vitamin A supplementation significantly reduced mortality; however, it is unclear whether these two treatment groups were similar at baseline (15). In Uganda and Zimbabwe, clinical trials are currently in progress that have been specifically designed to address the question whether vitamin A supplementation will reduce morbidity and mortality in HIV-infected infants and children.

Conclusion

Despite the lack of evidence that vitamin A supplementation can reduce vertical transmission of HIV, there is still an enormous burden of morbidity and mortality related to vitamin A deficiency in sub-Saharan Africa and other areas of the developing world. Control of vitamin A deficiency remains an important health intervention.

References

1. Tang AM, Graham NMH, Kirby AJ, et al. Dietary micronutrient intake and risk of progression to acquired immunodeficiency syndrome (AIDS) in human immunodeficiency virus type 1 (HIV-1)-infected homosexual men. *Am J Epidemiol* 1993; 138: 937–51.

2. Baum MK, Shor-Posner G, Lu Y, et al. Micronutrients and HIV-1 disease progression. *AIDS* 1995; 9: 1051–6.

3. Semba RD, Graham NMH, Caiaffa WT, et al. Increased mortality associated with vitamin A deficiency during human immunodeficiency virus type 1 infection. *Arch Intern Med* 1993; 153: 2149–54.

4. Semba RD, Miotti PG, Chiphangwi JD, et al. Maternal vitamin A deficiency and mother-to-child transmission of HIV-1. *Lancet* 1994; 343: 1593–7.

5. Greenberg BL, Semba RD, Vink PE, et al. Vitamin A deficiency and maternal-infant transmission of human immunodeficiency virus in two metropolitan areas in the United States. *AIDS* 1997; 11: 325–32.

6. Burger H, Kovacs A, Weiser B, et al. Maternal serum vitamin A levels are not associated with mother-to-child transmission of HIV-1 in the United States. *J Acquired Immune Defic Syndr Hum Retrovirol* 1997; 14: 321–6.

7. Burns DN, FitzGerald G, Semba RD, et al. Vitamin A deficiency and other nutritional indices during pregnancy in human immunodeficiency virus infection: prevalence, clinical correlates, and outcome. *Clin Infect Dis* 1999; 29: 328–34.

8. Semba RD, Miotti PG, Chiphangwi JD, et al. Infant mortality and maternal vitamin A deficiency during HIV infection. *Clin Infect Dis* 1995; 21: 966–72.

9. John GC, Nduati RW, Mbori-Ngacha D, et al. Genital shedding of human immunodeficiency virus type 1 DNA during pregnancy: association with immunosuppression, abnormal cervical or vaginal discharge, and severe vitamin A deficiency. *J Infect Dis* 1997; 175: 57–62.

10. Mostad SB, Overbaugh J, De Vange DM, et al. Hormonal contraception, vitamin A deficiency, and other risk factors

for shedding of HIV-1 infected cells from the cervix and vagina. *Lancet* 1997; 350: 922–7.

11. Nduati RW, John GC, Richardson BA, et al. Human immunodeficiency virus type 1-infected cells in breast milk: association with immunosuppression and vitamin A deficiency. *J Infect Dis* 1995; 172: 1461–8.

12. Coutsoudis A, Pillay K, Spooner E, et al. Randomized trial testing the effect of vitamin A supplementation on pregnancy outcomes and early mother-to-child HIV-1 transmission in Durban, South Africa. *AIDS* 1999; 13: 1517–24.

13. Fawzi WW, Msamanga GI, Spiegelman D, et al. Randomised trial of effects of vitamin supplements on pregnancy outcomes and T cell counts in HIV-1-infected women in Tanzania. *Lancet* 1998; 351: 1477–82.

14. Coutsoudis A, Bobat RA, Coovadia HM, et al. The effects of vitamin A supplementation on the morbidity of children born to HIV-infected women. *Am J Public Health* 1995; 85: 1076–81.

15 Fawzi WW, Mbise RL, Hertzmark E, et al. A randomized trial of vitamin A supplements in relation to mortality among human immunodeficiency virus-infected and uninfected children in Tanzania. *Pediatr Infect Dis J* 1999; 18: 127–33.

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About IVACG

Established in 1975, the International Vitamin A Consultative Group guides international activities for reducing vitamin A deficiency in the world. IVACG concentrates its efforts on stimulating and disseminating new knowledge, translating that new knowledge to enable its practical application, and providing authoritative policy statements and recommendations that others can use to develop appropriate prevention and control programs.

IVACG Steering Committee

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International Vitamin A Consultative Group (IVACG)

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